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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
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EXAMINER
LANDSMAN, ROBERT S

ART UNIT	PAPER NUMBER
1647	

DATE MAILED: 07/21/2003

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Applicati n No.	Applicant(s)	
	09/787,356	COCKS ET AL.	
	Examiner	Art Unit	
	Robert Landsman	1647	

-- The MAILING DATE of this communication appears n the c ver sh et with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☐ Responsive to communication(s) filed on _____ .

2a)☐ This action is **FINAL**. 2b)☒ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) 1-19 is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) 1-19 is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☒ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☒ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☒ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☒ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☒ Notice of References Cited (PTO-892)
2) ☒ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

1. Formal Matters

A. Preliminary Amendment A, filed 3/15/01, has been entered into the record.

B. Preliminary Amendment B, filed 6/25/01, has been entered into the record.

C. Claims 1-15 were pending in the application. In Amendment A, Applicants added new claims 16-19. Therefore, claims 1-19 are pending in this application and are the subject of this Office Action.

2. Title

The title of the invention is not descriptive. A new title is required that is clearly indicative of the invention to which the claims are directed. The following title is suggested, for example: Methods of treating airways diseases by activating PAR and agents useful for same.

3. Specification

A. The specification is objected to since it is not arranged properly. The following guidelines illustrate the preferred layout for the specification of a utility application. These guidelines are suggested for the applicant's use.

Arrangement of the Specification

As provided in 37 CFR 1.77(b), the specification of a utility application should include the following sections in order. Each of the lettered items should appear in upper case, without underlining or bold type, as a section heading. If no text follows the section heading, the phrase "Not Applicable" should follow the section heading:

(a) TITLE OF THE INVENTION.
(b) CROSS-REFERENCE TO RELATED APPLICATIONS.
(c) STATEMENT REGARDING FEDERALLY SPONSORED RESEARCH OR DEVELOPMENT.
(d) INCORPORATION-BY-REFERENCE OF MATERIAL SUBMITTED ON A COMPACT DISC (See 37 CFR 1.52(e)(5) and MPEP 608.05. Computer program listings (37 CFR 1.96(c)), "Sequence Listings" (37 CFR 1.821(c)), and tables having more than 50 pages of text are permitted to be submitted on compact discs.) or
REFERENCE TO A "MICROFICHE APPENDIX" (See MPEP § 608.05(a). "Microfiche Appendices" were accepted by the Office until March 1, 2001.)
(e) BACKGROUND OF THE INVENTION.
(1) Field of the Invention.
(2) Description of Related Art including information disclosed under 37 CFR 1.97 and 1.98.
(f) BRIEF SUMMARY OF THE INVENTION.

(g) BRIEF DESCRIPTION OF THE SEVERAL VIEWS OF THE DRAWING(S).
(h) DETAILED DESCRIPTION OF THE INVENTION.
(i) CLAIM OR CLAIMS (commencing on a separate sheet).
(j) ABSTRACT OF THE DISCLOSURE (commencing on a separate sheet).
(k) SEQUENCE LISTING (See MPEP § 2424 and 37 CFR 1.821-1.825. A "Sequence Listing" is required on paper if the application discloses a nucleotide or amino acid sequence as defined in 37 CFR 1.821(a) and if the required "Sequence Listing" is not submitted as an electronic document on compact disc).

B. The specification is objected to since the section containing the brief description of the drawings, starting on page 24, is inconsistent. First, certain Figures, such as, for example, Figure 5 and 8, comprise more than one Figure (e.g. A and B). However, the description is simply labeled "Figure 5" whereas other Figures, such as Figure 11 are labeled separately as "Figure 11a" and "Figure 11b." The labeling of the Figures with multiple "parts" or "panels" needs to be consistent.

C. Page 29/41 of the Figures is objected to since it is not in the proper order. This panel is labeled as Figure 38. However, there are two Figure 38's and it appears that this page (29/41) does not belong. The specification (Brief Description of the Drawings) should be amended accordingly.

D. Figure 35 is missing and there are two Figure 36's. It appears that the first Figure 36 should be labeled as "Figure 35."

E. This application does not contain an abstract of the disclosure as required by 37 CFR 1.72(b). An abstract on a separate sheet is required.

4. Claim Objections

A. The syntax of claim 6 can be improved by amending the claim to recite "SEQ ID NO:1, 2 and 3" instead of "Seq.I.D.<400>1..."

B. The syntax of claim 15 can be improved by placing a hyphen between the words PAR2 and "activating."

5. Claim Rejections - 35 USC § 112, first paragraph – scope of enablement

The following is a quotation of the first paragraph of 35 U.S.C. 112:

> The specification shall contain a written description of the invention, and of the manner and process of making and using it, in such full, clear, concise, and exact terms as to enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make and use the same and shall set forth the best mode contemplated by the inventor of carrying out his invention.

A. Claim 1-19 are rejected under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for methods of treating bronchoconstriction using TRAP and PAR2-AP, and compositions thereof, believed to be SEQ ID NO:1 and 2 of the present invention, does not reasonably provide enablement for methods and compositions for prophylaxis of bronchoconstriction or for treatment or prophylaxis of any and all airway diseases. The specification does not enable any person skilled in the art to which it pertains, or with which it is most nearly connected, to make the invention commensurate in scope with these claims.

In In re Wands, 8USPQ2d, 1400 (CAFC 1988) page 1404, the factors to be considered in determining whether a disclosure would require undue experimentation include (1) the quantity of experimentation necessary, (2) the amount of direction or guidance presented, (3) the presence or absence of working examples, (4) the nature of the invention, (5) the state of the prior art, (6) the relative skill of those in the art, (7) the predictability or unpredictability of the art, and (8) the breadth of the claims.

First, the breadth of the claims is excessive with regard to claiming a method for treating any and **all airway diseases** by activating PAR as well as for methods of preventing (**prophylaxis**) these diseases. Applicants have demonstrated that SFLLRN-NH2 and SLIGRL-NH2 can inhibit bronchoconstriction in various models (e.g. Figure 28). However, Applicants have not provided any guidance or working examples these ligands (or PARs) are capable of treating any and all airway diseases, including those of claim 5, nor have they demonstrated that they are able to *prevent* any and all airway diseases, including bronchoconstriction, in 100% of the population. Furthermore, it is not understood how, in claim 1, PAR activation to stimulate bronchoconstriction, would be able to treat, or prevent, airway diseases. Given this lack of guidance and working examples, it would not be predictable to the artisan how to treat any and all airway conditions, or how to prevent any and all airway conditions in 100% of the population, simply by activating PAR.

Furthermore, claims 6-9 recite "**functional equivalents, homologues and derivatives.**" Peptides which are "functional equivalents, homologues and derivatives" of the claimed peptides would have one or more amino acid substitutions, deletions, insertions and/or additions. Applicants provide no guidance or working examples of peptides which are functional equivalents, homologues and derivatives of the

claimed peptides, nor do they provide any guidance as to what critical residues are required to maintain the functional characteristics of the claimed full-length peptides. Furthermore, it is not predictable to one of ordinary skill in the art how to make a functional peptide other than the full-length peptides of the invention.

Finally, claims 10-19 are "reach through" claims. The breadth of the claims is excessive regarding claiming any and all "**compositions**" which can be used for bronchoprotection by modulating PAR. Applicants have only identified SEQ ID NO:1, 2 and 3 and have not provided any guidance or working examples for all compositions, which would include small organic and inorganic molecules, antibodies, antisense, etc., nor would it be predictable to the artisan how to make any and all activators of PAR, other than those disclosed in the specification. In addition, Applicants would not only not be enabled for compounds which affect bronchoconstriction, but would not be enabled for compounds which affect inflammation. Applicants have only provided guidance and working examples of compounds which affect bronchoconstriction, and have provided no guidance of how to treat inflammation.

In summary, the breadth of the claims is excessive with regard to Applicants claiming methods of treating or preventing any and all airway diseases, including the use of any and all compositions and peptides other than the full-length peptides of the invention. There is also a lack of guidance and working examples not only of the use of any compounds other than SFLLRN and SLIGRL, but a lack of guidance of treatment of any disease other than to inhibit bronchoconstriction. These factors, along with the lack of predictability to one of ordinary skill in the art as to how to make a functional peptide other that that of that of the full-length peptides of the invention, or of how to treat any and all airway diseases, or how to prevent any diseases, leads the Examiner to hold that undue experimentation is necessary to practice the invention as claimed.

6. Claim Rejections - 35 USC § 112, first paragraph – written description

A. Claims 6-19 are rejected under 35 U.S.C. 112, first paragraph, as containing subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the relevant art that the inventor(s), at the time the application was filed, had possession of the claimed invention.

These are genus claims. "**Functional equivalents, homologues and derivatives**" of the proteins of the invention would have one or more amino acid substitutions, deletions, insertions and/or additions to the proteins of SEQ ID NO:<400>1, <400>2 and <400>3. Similarly, Applicants have not provided adequate written description of any "**compositions**" other than the proteins of SEQ ID NO:1, 2 and 3.

The specification and claims do not indicate what distinguishing attributes are shared by the members of the genus. Thus the scope of the claims includes numerous structural variants, and the genus is highly variant because a significant number of structural differences between genus members is permitted. The specification and claims do not provide any guidance as to what changes should be made. Structural features that could distinguish compounds in the genus from others in the protein class are missing from the disclosure. No common structural attributes identify the members of the genus. The general knowledge and level of skill in the art do not supplement the omitted description because specific, not general, guidance is what is needed. Since the disclosure fails to describe the common attributes or characteristics that identify members of the genus, and because the genus is highly variant, SEQ ID NO:<400>1, <400>2 and <400>3 alone are insufficient to describe the genus. One of skill in the art would reasonable conclude that the disclosure fails to provide a representative number of species to describe the genus. Thus, Applicant was not in possession of the claimed genus at the time the invention was made.

7. Claim Rejections - 35 USC § 112, second paragraph

The following is a quotation of the second paragraph of 35 U.S.C. 112:

> The specification shall conclude with one or more claims particularly pointing out and distinctly claiming the subject matter which the applicant regards as his invention.

Claims 1-9 are rejected under 35 U.S.C. 112, second paragraph, as being indefinite for failing to particularly point out and distinctly claim the subject matter which applicant regards as the invention.

A. Claims 1-9 are confusing since the metes and bounds of "for a time" are not known. Zero seconds, or 3 milliseconds, respectfully, is a time and it is not understood how these times would be sufficient to treat, or prevent, an airway disease. Claims 2-9 are also rejected since they depend from claim 1.

B. Claims 13-19 are confusing since the metes and bounds of the term "activity" are not known. It is not clear what activity is being referred to, especially due to the recitation of "stimulates, induces or inhibits bronchoconstriction." In addition, it is confusing as to why the artisan would desire to stimulate or induce bronchoconstriction and inflammation. The claim would be clearer by reciting "said molecule inhibits bronchoconstriction..."

8. Claim Rejections - 35 USC § 102

The following is a quotation of the appropriate paragraphs of 35 U.S.C. 102 that form the basis for the rejections under this section made in this Office action:

> A person shall be entitled to a patent unless –
>
> (b) the invention was patented or described in a printed publication in this or a foreign country or in public use or on sale in this country, more than one year prior to the date of application for patent in the United States.

A. Claims 1, 3-6, 10-19 rejected under 35 U.S.C. 102(b) as being anticipated by Cicala et al. (Br. J. Pharmacol). The claims recite a method for a prophylaxis or treatment of an airway disease or inflammation by administering to an animal an agent capable of activating PAR as well as a composition comprising said agent. Cicala teach a method of modulating bronchial asthma in an animal by administering a composition comprising a PAR 1 receptor ligand, thrombin. The reference is silent as to how thrombin was produced or obtained. Regardless, the structure of thrombin is well-known in the art and has been both synthesized recombinantly as well as isolated. In addition, the reference is silent as to which tissue the thrombin has been obtained. Therefore, in absence of evidence to the contrary, thrombin would be expected to be isolated from airway epithelium, especially due to the fact that this agent mediates effects in this tissue. Claim 6 is included in this rejection since in the absence of any limitations to the terms "functional equivalents, homologs and derivatives," thrombin meets all these limitations. Furthermore, the reference is silent to the possibility that PAR 2 is being modulated. However, in absence of evidence to the contrary, it would be expected that PAR2 is being affected since the method of the present invention is inherently being performed, which would inherently be functioning via PAR2 in absence of evidence to the contrary.

9. Claim Rejections - 35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

A. Claims 1-19 are rejected under 35 U.S.C. 103(a) as being unpatentable over Cicala et al. Claims 1, 3, 5, 10, 11, 13 and 16-19 are recited in the above rejection under 35 USC 103. The claims also recite that the animal is human and that the PAR is PAR2. Cicala do not teach the use of a human, nor the use of PAR 2. However, it would have been obvious to one of ordinary skill in the art at the time of the present

invention to have used humans since humans also suffer bronchoconstriction and inflammation. Performing this method on humans would have been the next logical step. Modifying proteins in order to permit them entry across certain membrane barriers would have also been obvious since the location of the PARs are intracellular.

10. Conclusion

A. No claim is allowable.

Advisory information

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert Landsman whose telephone number is (703) 306-3407. The examiner can normally be reached on Monday - Friday from 8:00 AM to 5:00 PM (Eastern time) and alternate Fridays from 8:00 AM to 5:00 PM (Eastern time).

If attempts to reach the examiner by telephone are unsuccessful, the Examiner's supervisor, Gary Kunz, can be reached on (703) 308-4623.

Official papers filed by fax should be directed to (703) 308-4242. Fax draft or informal communications with the examiner should be directed to (703) 308-0294.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the Group receptionist whose telephone number is (703) 308-0196.

Robert Landsman, Ph.D.
Patent Examiner
Group 1600
July 17, 2003

ROBERT LANDSMAN
PATENT EXAMINER